Original Article

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TANAFFOS

Clinical Features and Outcomes of ICU Patients with COVID-19 Infection in Tehran, Iran: a Single-Centered Retrospective Cohort Study

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Background: The clinical characteristics of the novel coronavirus disease (COVID-19) were diverse and unspecific. Here, we identified the associated factors with surviving of COVID-19 ICU patients based on the clinical characteristics of patients admitted to one of the Corona Centre Hospitals of Iran.

Materials and Methods: This cohort study was performed retrospectively from February to June 2020 on 133 COVID-19 patients admitted to 4 intensive care units of Masih Daneshvari Hospital in Tehran, Iran. Demographic, medical, clinical manifestation at admission, laboratory parameters and outcome data were obtained from medical records. Also the SOFA and APACHE II scores were calculated. All data were analyzed using SPSS (version 23, IBM Corp.) software.

Results: The median (IQR) age of the patients was 62.0 (54.0-72.0) years in total. RT-PCR of throat swab SARS-CoV-2 in 80 patients (60.2%) was positive. Total mortality rate was 57.9 percent (77 patients). Dyspnea, hypertension and chronic pulmonary diseases were significantly common in non-survivors than survivors ($p<0.05$). Both SOFA and APACHE II scores were significantly higher in the non-survivors ($p<0.05$). Also other significant differences were observed in other parameters of the study.

Conclusion: The mortality rate of COVID-19 patients admitted to ICU is generally high. Dyspnea as initial presentation and comorbidity, especially hypertension and pulmonary diseases, may be associated with higher risk of severe disease and consequent mortality rate. Also, higher SOFA and APACHE II scores could indicate higher mortality in patients admitted to ICU.

Key words: Intensive Care Unit; COVID-19; Clinical features; Mortality

INTRODUCTION

Novel coronavirus pneumonia was first reported in late December 2019 in Wuhan, Hubei, China (1). Since then, the coronavirus disease 2019 (COVID-19) has spread rapidly across China and other countries, and the outbreak has become a worldwide concern and public health emergency (2). Until October 11 2020, more than 37 million confirmed cases and one million deaths from COVID-19 were

reported globally (3). In Iran, according to the latest epidemiologic data, at least 500,000 laboratory confirmed cases and 29,000 deaths of COVID-19 was reported until October 14, 2020 (3, 4); although the incidence of COVID-19 deaths tends to be higher in forthcoming future.

The pathogen is a novel betacoronavirus responsible for severe acute respiratory syndrome (SARS), named SARS-coronavirus 2 (SARS-CoV-2) (5). Coronaviruses are enveloped, single stranded RNA viruses with rapid mutation and recombination (6). The clinical characteristics of COVID-19 was diverse and unspecific, ranging from mild to severe respiratory, constitutional and gastrointestinal signs and symptoms, progresses to severe acute respiratory infection (SARI) and acute respiratory distress syndrome (ARDS) (1, 6, 7). The diagnosis is confirmed with approved real-time reverse transcriptase polymerase chain reaction (RT-PCR) test but with controversial sensitivity, and even chest radiologic modalities (6, 8-10).

Rapid spread of the disease and increasing number of new cases signifies the need for better understanding of clinical and para-clinical characteristics of COVID-19, which helps in prompt triage and management of patients. Here, we identified the associated factors with surviving of COVID-19 ICU patients based on the clinical characteristics of patients admitted to one of the Corona Centre Hospitals, Tehran, Iran.

MATERIALS AND METHODS

Study design and patients

This cohort study was performed retrospectively from February to June 2020 on patients admitted to 4 intensive care units of Masih Daneshvari Hospital in Tehran, Iran. This hospital was the designated as the Corona Center Hospital to treat SARS-CoV-2 pneumonia from the initial days of corona epidemics. All patients admitted to ICUs with diagnosis of SARS-CoV-2 pneumonia according to WHO interim guidance were enrolled in this study (11). The study was approved by Masih Daneshvari Hospital Ethics Committee (IR.SBMU.NRITLD.REC.1399.033). Informed consent was obtained from conscious patients or first degree relatives, if any patient was unconscious.

Procedure

During the first days of detection of the novel coronavirus, due to limitations in definite diagnosis based on reverse transcriptase-polymerase chain reaction (RT-PCR) method, the definite SARS-CoV-2 diagnosis was made on the basis of available guidance and reports from involved countries, in addition to PCR results. The initial diagnosis is mainly based on clinical presentations and status, primary laboratory tests, and imaging findings (chest radiography and chest computed tomography) according to World Health Organization (WHO) and Ministry of Health guidelines as well as ruling out other common microbial respiratory infections including influenza infection. Laboratory confirmation of COVID-19 was done in virology lab of Masih Daneshvari Hospital using RT-PCR.

All suspected individuals underwent chest radiography and primary laboratory investigations. Chest CT scan and complementary laboratory test were done when severe pneumonia was presented and admission indicated. Based on WHO and Ministry of Health interim protocols throat swab specimen was obtained from all patients at the time of admission. Of 174 suspected cases referred for admission to the intensive care units from mid-February, 41 patients were excluded due to other diagnoses, inconclusive data, incomplete data or cardio respiratory arrest at the time of admission and finally 133 patients diagnosed with SARS-CoV-2 infection were enrolled in this study (Figure 1). Patients underwent supportive care or invasive procedures, if indicated. In order to evaluate viral clearance in patients before discharging them from ICUs, repeated tests for SARS-CoV-2 as well as laboratory and imaging evaluation was done.

Data collection

Demographic, medical, clinical manifestation at admission, para-clinical (including imaging and laboratory) parameters and outcome data were obtained retrospectively from medical records of patients. Patients

were followed-up for clinical outcomes. Missing data were obtained from attending physician or health care providers directly, if needed. For some epidemiologic and medical data that were not available in medical records, direct questioning from conscious patients or relatives of unconscious patients was done. To double check the data, two physicians independently checked all the data. All data were collected and compared between non-survivors and survivors admitted to ICUs with diagnosis of SARS-CoV-2 pneumonia, as outcome variable.

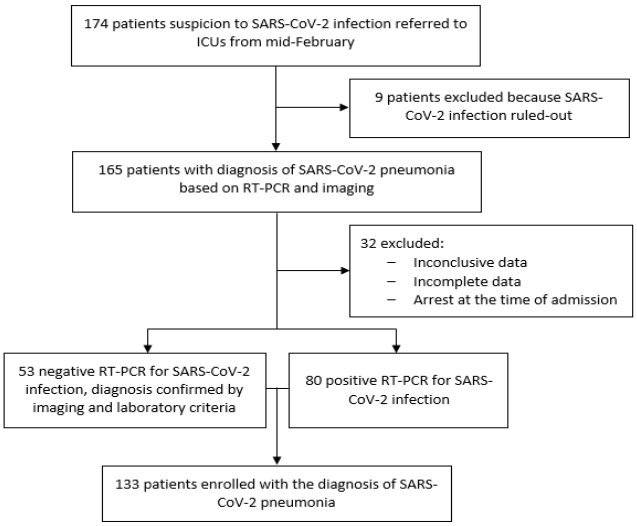

Figure 1. Study flow diagram. SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. ICU = intensive care unit. RT-PCR = reverse transcriptase-polymerase chain reaction.

We also calculated sepsis-related organ failure assessment (SOFA) and APACHE II score to predict and estimate mortality in patients admitted to the ICU, based on clinical data and laboratory values (12, 13).

Statistical Analysis

All continuous variables were presented as the median (IQR), and categorical variables were presented as N (%), using SPSS (version 23, IBM Corp.) software. Chi-square and Mann–Whitney U tests were used to analyse categorical and continuous data, respectively. A p-value less than 0.05 was considered to denote statistical significance.

RESULTS

In current study, 133 patients with diagnosis of SARS-CoV-2 pneumonia were considered as eligible for inclusion. The median (IQR) age of the patients was 62.0 (54.0-72.0) years in total, 61.0 (45.5-68.0) years in survivors and 64.0 (56.0-73.0) years in non survivors. 88 patients (64.4%) were male and 45 (33.8%) were female. The differences between survivors and non-survivors regarding age (p=0.135) and sex (p=0.061) were not significant (Table 1). The survivors and non-survivors in each age group is summarized in Table 1. Total mortality rate was 57.89 percent (77 patients).

88 patients (66.2%) had chronic medical illness, of which 34 (60.7%) patients were in survivors group and 54 (70.1%) in non-survivors group. Most common chronic medical illness was diabetes mellitus, hypertension, chronic pulmonary diseases and cardiovascular diseases with prevalence of 62 (46.6%), 65 (48.9%), 21 (15.8%) and 26 (19.5%) among patients, respectively. Hypertension and chronic pulmonary diseases were significantly more common in non-survivors than survivors (p<0.05). Among the patients, only 6 (4.5%) were using immunosuppressive medications (Table 1).

At the onset of illness, the most common signs/symptoms among patients was dyspnea (84.2%), fever (69.2%), and cough (61.7%) which was mostly dry cough. The frequency of dyspnea was significantly higher in non-survivors compared to survivors (Table 2). Other presentations included constitutional symptoms (such as chill, myalgia, malaise, sweating and anorexia). The triad of fever, dyspnea, and cough was observed in 33 patients (42.9%) of non-survivors and 17 patients (30.4%) of survivors (Table 2) group. The median (IQR) of vital signs including temperature, respiratory rate (RR), heart rate (HR), systolic and diastolic blood pressure are presented in Table 3. The median of RR and O2 saturation was significantly higher and lower in non-survivors compared to survivors, respectively (p<0.05, Table 3).

Table 1. Demographics and characteristics of patients admitted to Masih Daneshvari Hospital with SARS-CoV-2 pneumonia. Data are mean (SD) or number (%)

Demographic/characteristics	Total (n=133)	Survivors (n=56)	Non-survivors (n=77)	p-value
Age, year				
Median (IQR)	62 (54-72)	61 (45.5-68)	64 (56-73)	
<30	6 (4.5%)	3 (5.4%)	3 (3.9%)	
30-39	10 (7.5%)	8 (14.3%)	2 (2.6%)	0.135
40-49	12 (9%)	4 (7.1%)	8 (10.4%)	0.204
50-59	27 (20.3%)	8 (14.3%)	19 (24.7%)	
60-69	40 (30.1%)	21 (37.5%)	19 (24.7%)	
≥70	38 (28.6%)	12 (21.4%)	26 (33.8%)	
Sex				
Male	88 (66.2%)	32 (57.1%)	56 (72.7%)	0.061
Female	45 (33.8%)	24 (42.9%)	21 (27.3%)	
Chronic medical illness	88 (66.2%)	34 (60.7%)	54 (70.1%)	0.257
Diabetes mellitus	62 (46.6%)	24 (42.9%)	38 (49.4%)	0.459
Hypertension	65 (48.9%)	21 (37.5%)	44 (57.1%)	0.025
Chronic pulmonary disease	21 (15.8%)	4 (7.1%)	17 (22.1%)	0.020
Cardiovascular disease	26 (19.5%)	11 (19.6%)	15 (19.5%)	0.981
CKD	9 (6.8%)	2 (3.6%)	7 (9.1%)	0.093
Liver disease	4 (3.0%)	3 (5.4%)	1 (1.3%)	0.176
Neurologic disease	10 (7.5%)	4 (7.1%)	6 (7.8%)	0.888
Rheumatologic disease	5 (3.8%)	3 (5.4%)	2 (2.6%)	0.409
Immunosuppressant	6 (4.5%)	4 (7.1%)	2 (2.6%)	0.212
BMI ≥ 35	13 (16.3%)	4 (12.1%)	9 (19.1%)	0.402
Smoker	22 (16.5%)	7 (12.5%)	15 (19.5%)	0.285

Table 2. The frequency of sign/symptom at admission*

Sign/symptom	Total (n=133)	Survivors (n=56)	Non-survivors (n=77)	p-value
Dyspnea	112 (84.2%)	41 (73.2%)	71 (92.2%)	0.003
Fever	92 (69.2%)	36 (64.3%)	56 (72.7%)	0.298
Cough	82 (61.7%)	33 (58.9%)	49 (63.6%)	0.581
Dry	65 (79.3%)	23 (69.7%)	42 (85.7%)	0.079
Productive	17 (20.7%)	10 (30.3%)	7 (14.3%)	
Chill	70 (52.6%)	30 (53.6%)	40 (51.9%)	0.853
Myalgia	60 (45.1%)	21 (37.5%)	39 (50.6%)	0.132
Malaise	51 (38.3%)	18 (32.1%)	33 (42.9%)	0.210
Sweating	34 (25.6%)	13 (23.2%)	21 (27.3%)	0.596
Anorexia	39 (29.3%)	14 (25%)	25 (32.5%)	0.350
Nausea/vomiting	18 (13.5%)	8 (14.3%)	10 (13%)	0.829
Chest Pain	18 (13.5%)	7 (12.5%)	11 (14.3%)	0.766
Headache	16 (12%)	6 (10.7%)	10 (13%)	0.691
Pharyngalgia	23 (17.3%)	10 (17.9%)	13 (16.9%)	0.883
Confusion	22 (16.5%)	8 (14.3%)	14 (18.2%)	0.550
Dizziness	10 (7.5%)	3 (5.4%)	7 (9.1%)	0.420
Diarrhea	14 (10.5%)	3 (5.4%)	11 (14.3%)	0.098
Rhinorrhea	17 (12.8%)	7 (12.5%)	10 (13%)	0.934
Hemoptysis	7 (5.3%)	4 (7.1%)	3 (3.9%)	0.408
Vertigo	13 (9.8%)	4 (7.1%)	9 (11.7%)	0.383
Seizure	3 (2.3%)	1 (1.8%)	2 (2.6%)	0.756
Triad of fever, cough and dyspnea	50 (37.6)	17 (30.4)	33 (42.9)	0.098

*Data are number (%)

Table 3. Vital signs at the time of admission. Data are median (IQR)

Vital sign (at admission)	Total (n=133)	Survivors (n=56)	Non-survivors (n=77)	p-value
Temperature	37.30 (37.0-37.90)	37.25 (37.0-37.90)	37.3 (37.0-38.0)	0.903
Respiratory rates	20.0 (18.00-22.00)	18.00 (18.0-21.0)	20.0 (18.0-24.0)	0.021
Heart rate	92.0 (80.00-102.00)	90.50 (80.0-108.5)	92.0 (80.0-100.0)	0.967
Systolic blood pressure	130.0 (120.00-141.00)	131.00 (120.50-142.50)	130.0 (119.0-141.0)	0.252
Diastolic blood pressure	80.0 (70.00-85.00)	80.0 (74.5-89.5)	78.0 (70.0-83.0)	0.154
Saturation of O2	77.0 (70.0-88.0)	82.5 (73.50-90.0)	74.0 (65.0-87.0)	0.003

The RT-PCR of throat swab SARS-CoV-2 was positive in 80 patients (60.2%), but patients with negative RT-PCR results met other diagnostic criteria for SARS-CoV-2 pneumonia, including laboratory and radiological investigations (Table 2). The median (IQR) of white blood cells (WBC) count was significantly higher in non-survivors compared to survivors. However, only 55/133 (41.4%) patients had increased leukocyte count (more than $10x10^9$ per liter). The median (IQR) of lymphocyte count was slightly, but not significantly higher in survivors (P=0.36) and polymorphonuclear (PMN) count was significantly higher in non-survivors (p<0.001). Other hematologic indices are summarized in Table 4. Furthermore, the median of blood urea nitrogen (BUN) was higher in non-survivors compared to survivors (15.17 vs. 11.24 mmol/L, respectively, p<0.05). Additionally, the median (IQR) of creatinine was 106.19 (88.50-123.89) µmol/L totally, 97.35 (88.50-106.19) µmol/L in survivors and 106.19 (92.92-141.59) µmol/L in non-survivors, which was significantly higher in the latter group (p=0.008). The median and frequency of raised hepatic enzymes is shown in Table 4. As noted in the table, the median of aspartate aminotransferase (AST) was higher in non-survivors compared to survivors (47.50 vs. 36.0 IU/L, respectively, p=0.005). Also, raised (>105 IU/L) alkaline phosphatase (ALKP) occurred more frequently in non-survivors (p=0.01).

The median (IQR) of lactate dehydrogenase (LDH) was 543.00 (426.00-853.50) IU/L in non-survivors and 852.00 (624.00-1074.00) IU/L in survivors, which is significantly higher in latter group (p<0.001). Moreover, the number of patients with LDH levels of more than 500 IU/L in non-survivors was significantly more than survivors (72/77 vs. 34/56, respectively, p<0.001). Also, the median of magnesium in non-survivors was higher in comparison to the survivors (p<0.001, Table 4). All other serologic values are summarized in Table 4.

Based on available data, the median (IQR) duration of hospitalization in our study was 7.0 (4.0-13.0) days in total, and was 8.50 (5.0-16.5) and 6.00 (3.0-11.0) day in survivors and non-survivors, which was significantly higher in survivors compared to non-survivors (p<0.05). However, the duration of ICU stay in the current study was not significantly different in survivors, in comparison to non-survivors (p=0.25, table 6). On the other hand, the time from onset of symptoms to hospitalization was significantly higher in non-survivors than in survivors (p<0.001, table 5). The median (IQR) scores of SOFA and APACHE II in all patients were 5.0 (4.0-7.0) and 9.0 (6.0-13.0) respectively, and both were significantly higher in non-survivors than survivors (p<0.05, table 6).

Table 4. Laboratory findings of patients infected with SARS-CoV-2 pneumonia. Data are median (IQR) or n/N (%), where N is the total number of patients with available *data.*

Laboratory findings	Total (n=133)	Survivors (n=56)	Non-survivors (n=77)	p-value
COVID-19 RT-PCR				
Positive	80 (60.2%)	27 (48.2%)	53 (68.8%)	-
Negative	53 (39.8%)	29 (51.8%)	24 (31.2%)	0.016
WBC (10^9/L)	9.02 (6.50-13.00)	7.21 (5.05-11.10)	10.10 (7.73-13.65)	<0.001
<4.0	8/133 (6.0%)	6/56 (10.7%)	2/77 (2.6%)	
4.0-10.0	70/133 (52.6%)	34/56 (60.7%)	36/77 (46.8%)	0.014
>10.0	55/133 (41.4%)	16/56 (28.6%)	39/77 (50.6%)	
Lymph (10^3/mm^3)	0.93 (0.70-1.40)	1.05 (73.90-151.60)	0.86 (69.25-124.32)	0.360
<1.0	69/133 (51.9%)	27/56 (48.2%)	42/77 (54.5%)	0.471
≥1.0	64/133 (48.1%)	29/56 (51.8%)	35/77 (45.5%)	
PMN (10^3/mm^3)	7.43 (4.97-11.19)	5.53 (376.98-895.70)	8.86 (611.10-1200.67)	<0.001
RBC (10^{12}/L)	4.55 (4.11-5.03)	4.43 (4.10-5.02)	4.57 (4.14-5.03)	0.715
Hemoglobin (mg/dl)	13.20 (12.20-14.60)	13.20(12.15-14.55)	13.20 (12.20-14.60)	0.861
MCV (fL)	85.90 (82.30-88.80)	86.35 (81.40-89.60)	85.60 (82.60-88.50)	0.800
Platelets (10^9/L)	197.00 (140.00-261.00)	184.00 (134.50-261.00)	197.00 (150.00-261.00)	0.352
<100	15/133 (11.3%)	8/56 (14.3%)	7/77 (9.1%)	0.350
≥100	118/133 (88.7%)	48/56 (85.7%)	70/77 (90.9%)	
BUN (mmol/L)	39.00 (29.00-67.00)	11.79 (9.82-15.54)	16.43 (11.79-28.93)	0.005
<2.8	0	0	0	
2.8-8.1	16/133 (12.0%)	6/56 (10.7%)	10/77 (13.0%)	0.691
>8.1	117/133 (88.0%)	50/56 (89.3%)	67/77 (87.0%)	
Creatinine (µmol/L)	106.19 (88.50-123.89)	97.35 (88.50-106.19)	106.19 (92.92-141.59)	0.008
<133.0	106/133 (79.7%)	50/56 (89.3%)	56/77 (72.7%)	0.019
≥133.0	27/133 (20.3%)	6/56 (10.7%)	21/77 (27.3%)	
AST (IU/L)	45.00 (32.00-69.50)	38.00 (28.00-57.00)	50.00 (35.00-79.00)	0.005
≤40	55/133 (41.4%)	31/56 (55.4%)	24/77 (31.2%)	0.005
>40	78/133 (58.6%)	25/56 (44.6%)	53/77 (68.8%)	
ALT (IU/L)	34.50 (20.00-52.00)	34.00 (20.00-47.00)	36.00 (22.00-59.00)	0.319
≤50	97/133 (72.9%)	44/56 (78.6%)	53/77 (68.8%)	0.212
>50	36/133 (27.1%)	12/56 (21.4%)	24/77 (31.2%)	
ALKP (IU/L)	176.00 (143.00-231.00)	174.50 (145.50-222.50)	180.00 (141.00-239.00)	0.464
<105	7/133 (5.3%)	6/56 (10.7%)	1/77 (1.3%)	0.016
≥105	126/133 (94.7%)	50/56 (89.3%)	76/77 (98.7%)	
LDH (IU/L)	785.50 (534.00-1003.00)	543.00 (426.00-853.50)	852.00 (624.00-1074.00)	<0.001
<225	0	0	0	
225-500	27/133 (20.3%)	22/56 (39.3%)	5/77 (6.5%)	<0.001
>500	106/133 (79.7%)	34/56 (60.7%)	72/77 (93.5%)	
Sodium (mmol/L)	139.00 (136.00-140.00)	139.00 (137.00-140.00)	138.00 (136.00-141.00)	0.469
Potassium (mmol/L)	4.20 (3.90-4.50)	4.25 (3.90-4.60)	4.00 (3.70- 4.50)	0.125
Magnesium (mmol/L)	2.20 (2.00-2.40)	2.10 (1.90-2.20)	2.30 (2.10-2.40)	0.001
Prothrombin Time (second)	13.60 (13.00-15.00)	13.50 (12.80-14.50)	14.00(13.00-15.30)	0.162
INR	1.28(1.17-1.55)	1.26 (1.13-1.45)	1.35 (1.17-1.59)	0.164
Partial Thromboplastin Time	43.00 (37.00-48.00)	42.00 (34.50-47.50)	43.00 (38.00-48.00)	0.215

Table 5. Duration of hospitalization. Data are median (IQR).

Hospitalization	Total (n=133)	Survivors (n=56)	Non-survivors (n=77)	Total (n=133)
Days in Hospital	7.0 (4.0-13.0)	8.50 (5.0-16.5)	6.00 (3.0-11.0)	0.025
Days in ICU	5.0 (3.0-8.0)	5.00 (3.0-8.0)	4.00 (2.0-8.0)	0.252
Days from Symptom Onset to hospitalization	7.0 (5.0-10.0)	6.00 (4.0-7.0)	8.00 (5.0-11.0)	<0.001

Table 6. SOFA and APACHE II Scores. Data are median (IQR).

Scores	Total (n=133)	Survivors (n=56)	Non-survivors (n=77)	Total (n=133)
SOFA	5.0 (4.0-7.0)	4.5 (4.0-5.5)	5.0 (4.0-7.0)	0.010
APACHE II	9.0 (6.0-13.0)	8.0 (4.0-10.5)	10.0 (6.0-14.0)	0.007

DISCUSSION

Here we described 133 critically ill patients with SARS-CoV-2 pneumonia. 77 (57.89%) of patients died in ICUs and other patients were recovered or discharged from ICUs. The main treatment plan for SARS-COV-2 pneumonia is supportive care, since there is no specialized and confirmed treatment introduced yet. However, aggressive treatment is needed to treat critically ill patients. Patients with hypoxemia and respiratory distress suggestive of severe ARDS required mechanical ventilation. All patients were isolated during treatment. Also non-critical patients could be treated with close follow-up, until the symptoms resolved or further management was needed (14, 15).

SARS-CoV-2 infection can be transmitted through human-to-human contact, and the mortality rate is generally considered lower than other related infections such as SARS and MERS. Though, in our study, the mortality rate of critically ill patients was higher than SARS infection (16-18). This was in line with most critical care-based studies (19, 20). Many epidemiological features, clinical manifestations and symptom of the SARS-CoV-2 are similar to SARS infection (21, 22).

Initially, the main pathophysiology of SARS-CoV-2 is severe acute respiratory distress syndrome (ARDS). Previous evidence about SARS pathophysiology suggested that increases in serum pro-inflammatory cytokines including interleukin-1 beta (IL-1β), IL-6 and interferon-γ (IFN-γ) reflects inflammatory pulmonary damage (23, 24). Additionally, some other pathophysiologic conditions were proposed for SARS-CoV-2 among critical patients. Huang et al. showed that patients with SARS-CoV-2 infections had higher level of proinflammatory cytokines such as IL-1β, IFN-γ, monocyte chemoattractant protein 1 (MCP1) and inducible protein 10 (IP10), which mediates T-helper 1 activity. They demonstrated that cytokine storm can serve as underlying pathophysiology of organ damage and associated with disease severity (1). However, using corticosteroids in patients with SARS and MERS can delay viral clearance and lacks benefits (25, 26). Although the utility of corticosteroid therapy in patients with COVID-19 was controversial (27), benefits of dexamethasone usage was promising (28).

Human-to-human transmission of SARS and MERS has occurred in hospital and health care setting, and viral shedding does not occur until symptoms develop (29). But for novel coronavirus, there are some reports that viral shedding occurs days before the onset of disease symptoms (30-32). Chan et al. argued that incubation period of SARS-CoV-2 is the same as SARS, and attack rate is up to 83%, by study of a family cluster (6).

The number of men who died from the disease is two times higher than women in our study. However, in this study the infected males were approximately two times higher than females. Primary studies indicated that nearly 70% of patients infected with SARS-CoV-2 were male (1, 15). The median age of patients admitted to ICUs was 62 (IQR 57-72) years. Underlying diseases and comorbidities may be associated with SARS-CoV-2 infection mortality (14, 15). In the present study, the number of patients with

chronic medical illnesses that died from COVID-19 was more than survivors. Most prevalent comorbidities were diabetes mellitus, hypertension and pulmonary disease.

Previously, de Wit et al. demonstrated that comorbid condition, advanced age and male sex have an important role in severe complication and mortality of SARS and MERS (29). Other primary studies have shown that the mortality rate of SARS-CoV-2 was similar to what was reported for ARDS (33, 34). This was confirmed in our study with 57.89% of mortality in SARS-CoV-2 patients.

Clinical presentations in patients requiring hospitalization are non-specific and identical with moderate to severe pneumonia (1, 35, 36). The most common symptom in our study was dyspnea, including 84.2% of the patients at the time of admission, and fever and cough in second and third places. These findings are in accordance with other reports regarding SARS-CoV-2 pneumonia (1, 15, 34, 37). All individuals should not necessarily have the triad of fever, dyspnea and cough at the time of admission. Evidence indicated that patients may be afebrile at presentation, and the onset of fever may be delayed until worsening of respiratory symptoms, at least 2-8 days later (6, 34, 38). This suggested that asymptomatic patients are the main source of spread of infection causing a large-scale outbreak.

The presence of dyspnea was considerably higher in non-survivors than survivors. The triad of fever, dyspnea and cough was present in nearly 38% of the patients, and this was more prevalent in non-survivors. This triad was reported previously as main symptoms of SARS-C0V-2 pneumonia (1). Gastrointestinal involvement has been shown in coronaviruses infections (39). The incidence of diarrhea in SARS and MERS infections was reported as 10-30% (40, 41). However, in our study, 14 patients (10.5%) had diarrhea.

In our study, about 60% of the patients had positive RT-PCR for SARS-CoV-2. For whom the PCR results were negative, diagnosis of SARS-CoV-2 was based mainly on clinical manifestations or imaging findings. Chan et al. suggested that lower respiratory tract sample has higher viral load than upper tract in SARS-CoV-2 infections (6), consistent with findings on MERS infections (42). This can be responsible for negative result in infected patients, in addition to the variable sensitivity of detection kits.

As for laboratory investigations, the median of leukocyte count was significantly higher among non-survivors. In our patient population, leukopenia (WBC<$4x10^9$ per liter) occurred in six patients that had survived SARS-CoV-2 pneumonia and were discharged from ICUs, while only two patients who expired in ICU, had leukopenia. Other studies reported lymphopenia as a prominent finding in critical patients. Yang et al. reported that more than 80% of the patients in critical setting had lymphocytopenia (34). This finding in SARS and MERS was due to the invasion of T-cell lymphocytes by the virus and activation of apoptosis pathways (43, 44). However, the difference regarding frequency of lymphopenia was not significant in survivors and non-survivors, but PMN count was significantly higher in non-survivors.

Blood urea nitrogen was increased in approximately 90% of patients (more than 8.1 mmol per liter). The median of blood urea was significantly higher in non-survivals. However, the median of creatinine was in upper limits of normal values in this study, only 27 patients had levels above the 133.0 umol per liter. This could be indicative of renal damage. Furthermore, LDH is an indicative of organ failure in critical setting. In our study the median level of LDH was increased among patients, and all of patients had levels above normal values. Patients who have died from SARS-CoV-2 infection have considerable increase in LDH compared to survived patients. This finding could be attributed to severe organ damage. Additionally, almost all patients had ALKP levels above the normal values.

Interestingly, the median of magnesium level in this study was above the normal limit, and non-survivor patients had higher levels of magnesium than survivors. However, it is not clear that this finding is the consequence or result of organ failure in our patients, as magnesium has intracellular storage and renal clearance. Various studies emphasized the association between hypermagnesemia

and higher rate of mortality in critical patients (45-48). Haider et al. demonstrated that hypermagnesemia is a strong independent risk factor for higher mortality among critical patients (45). Consistently, Naksuk et al. concluded that magnesium level above 0.99 mmol/L in intensive cardiac care unit (ICCU) patients is associated with higher in-hospital mortality, even after adjustment for other risk factor that may alter cardiac function (46).

Furthermore, the predictive scores of mortality in ICU patients using SOFA and APACHE II scoring system was significantly higher in non-survivor patients, as expected. The total duration of hospitalization was significantly lower in non-survivors, but not the duration in ICU care. However, the duration of time from onset of the symptoms to hospitalization was significantly higher in patients who died from the disease, which may indicate long-lasting duration of disease presentation in these individuals or late referral to health care facilities.

Radiologic findings usually include diffuse or multifocal consolidation, pneumonic changes in most of patients suggestive a viral pneumonia (6). Imaging characteristics of SARS-CoV-2 pneumonia are also similar to SARS pneumonia (49, 50). However, reports noted that at the beginning of the disease course, patients may have normal CXR despite chest involvement as shown by chest CT (51, 52). Thus, chest CT has higher sensitivity than CXR. Song et al. reported that ground glass opacities were seen in more than 75% of the patients, along with interstitial and/or interlobular septal thickening (53). Ng et al. introduced ground glass opacities and consolidation in the lung periphery as SARS-CoV-2 imaging hallmarks (51). Consistent findings were demonstrated in other studies (54-57). A study by Chen et al. on 99 patients with SARS-CoV-2 pneumonia in Wuhan, China revealed that 75% of patients had bilateral pneumonia and 14% had multiple mottling and ground glass opacities, based on CXR and chest CT (15). Huang et al. have shown that 98% of 41 critically ill patients had bilateral involvement based on CT findings. They argued that the typical findings in their study population were bilateral multiple lobular and subsegmental consolidation (1). In our study, more than 90% of the patients had bilateral and diffuse lung involvement based on CXR. All patients who died from the pneumonia had bilateral involvement. These findings are similar with previous studies.

The current study has faced several limitations. First, the sample size of patients was small. We included almost all patients admitted to ICUs of Masih Daneshvari Hospital, but relatively small sample size limited risk and prognosis assessment. Second, the specimen for RT-PCR was taken from throat. Paired specimen from lower respiratory tract or repeated sample taking may decrease negative results of RT-PCR. This was a preliminary, hospital-based report from Iran and more cohort studies, both community and outpatient setting, are needed for confirming our findings.

CONCLUSION

The mortality rate of patients admitted to ICU is generally high. The comorbidity, especially hypertension and pulmonary diseases may be associated with higher risk of severe disease and consequent mortality rate. Also, dyspnea as initial presentation may indicate more diffuse and severe SARS-CoV-2 infections .

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Conflict of interest

The authors declare that they have no conflict of interest.

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